Remarks

Claims 26-33 are pending in the subject application and currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Applicant gratefully acknowledges the Examiner's withdrawal of the rejection under 35 U.S.C. § 103(a).

Claims 26-33 have been rejected under 35 U.S.C. § 101 on the basis that the claimed invention is not supported by a credible asserted utility or a well-established utility. Claims 26-33 have also been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Office Action argues that "to ask a patient to sit through at least fifteen minutes and up to two hours of heat treatment at a level that simulates a condition that potentially ranges from a moderate fever to a temperature sufficient to trigger heatstroke would be to place an intolerable burden on that patient." This argument appears to be based upon an alleged "safety issue" more properly addressed by the Food and Drug Administration (FDA) review process. No other rationale for rejecting the claims as unsupported by a credible asserted or well-established utility is articulated in the Office Action. Applicant respectfully submits that the grounds of rejection fail to establish that claimed invention lacks a patentable utility and withdrawal of the rejection is respectfully submitted.

As the Patent Office is aware, a claimed invention is properly rejected under 35 U.S.C. § 101 only if the Patent Office (a) makes a *prima facie* showing that the claimed invention lacks utility, and (b) provides sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing. *In re Gaubert*, 524 F.2d 1222, 1224, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975) ("Accordingly, the PTO must do more than merely question operability it must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability."). If the Office cannot develop a proper *prima facie* case and provide evidentiary support for a rejection under 35 U.S.C. § 101, a rejection on this ground should not be imposed. See, *e.g.*, *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992) ("[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant.... If examination at the initial stage does not produce a *prima facie*

case of unpatentability, then without more the applicant is entitled to grant of the patent."). See also *Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985) (applying *prima facie* case law to 35 U.S.C. 101); *In re Piasecki*, 745 F.2d 1468, 223 U.S.P.Q. 785 (Fed. Cir. 1984). As stated in the Manual of Patent Examining Procedure at §2107.02(IV),

> The *prima facie* showing must be set forth in a well-reasoned statement. Any rejection based on lack of utility should include a detailed explanation why the claimed invention has no specific and substantial credible utility. Whenever possible, the examiner should provide documentary evidence regardless of publication date (e.g., scientific or technical journals, excerpts from treatises or books, or U.S. or foreign patents) to support the factual basis for the *prima facie* showing of no specific and substantial credible utility. If documentary evidence is not available, the examiner should specifically explain the scientific basis for his or her factual conclusions.

Applicant also submits that the Federal Circuit has repeatedly stated that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs or methods to be used in the United States. FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. *Scott [v. Finney]*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 [(Fed. Cir. 1994)]. Accordingly, the courts have stated that Patent Office personnel should not construe 35 U.S.C. § 101, under the logic of "practical" utility or otherwise, to require that an applicant demonstrate that a therapeutic agent based on a claimed invention is a safe or fully effective drug for humans. See, *e.g.*, *In re Sichert*, 566 F.2d 1154, 196 U.S.P.Q. 209 (C.C.P.A. 1977); *In re Hartop*, 311 F.2d 249, 135 U.S.P.Q. 419 (C.C.P.A. 1962); *In re Anthony*, 414 F.2d 1383, 162 U.S.P.Q. 594 (C.C.P.A. 1969); *In re Watson*, 517 F.2d 465, 186 U.S.P.Q. 11 (C.C.P.A. 1975). These general principles are equally applicable to situations where an applicant has claimed a process for treating a human or animal disorder. In such cases, the asserted utility is usually clear—the invention is asserted to be useful in treating the particular disorder. If the asserted utility is credible, there is no basis to challenge such a claim on the basis that it lacks utility under 35 U.S.C. § 101.

The subject invention is directed to methods for preventing chemotherapy-induced hair loss (alopecia) by administering an effective heat dose to the scalp of the patient or other region

susceptible to chemotherapy-induced hair loss prior to the administration of a chemotherapeutic drug. As pointed out in the as-filed specification, chemotherapy frequently induces hair loss and a number of methods and devices have been developed in an effort to reduce or prevent the loss of hair (see as-filed specification at pages 1-2). For example, scalp tourniquets have been used to treat chemotherapy-induced alopecia (although the effectiveness of their use has not been unambiguously demonstrated, see specification, page 1, lines 19-23). Scalp hypothermia, practiced primarily in Europe, has also been used for reducing or preventing chemotherapy induced hair loss (although the results have remained notoriously variable, see specification, page 1, lines 23-27). Thus, methods of, and approaches to, reducing, preventing, or protecting a patient or individual against chemotherapy-induced hair loss are clearly considered to be of practical or well-established, substantial, specific and credible usefulness (utility) by those skilled in the art treating patients or individuals with chemotherapeutic drugs.

Against this legal and factual framework, Applicant respectfully submits that the Patent Office has failed to establish a *prima facie* case that the claimed invention lacks utility. For example, there has been no evidentiary basis provided for challenging the asserted utility of the claimed invention by the Patent Office nor has a well-reasoned statement or detailed explanation as to why the claimed invention lacks utility been provided by the Patent Office. The only grounds articulated for rejecting the claims as lacking patentable utility is the view that "to ask a patient to sit through at least fifteen minutes and up to two hours of heat treatment at a level that simulates a condition that potentially ranges from a moderate fever to a temperature sufficient to trigger heatstroke would be to place an intolerable burden on that patient." Applicant respectfully submits that this "view" is insufficient to reject the claimed invention as lacking patentable utility and fails to satisfy the legal requirements necessary for rejecting the claims as lacking a patentable utility and reconsideration and withdrawal of the rejection is respectfully requested.

The Office Action has also rejected claims 26-33 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. In articulating the grounds of rejection, the Office Action argues that "[i]n methods of treating a condition, a time-dependence factor must be taken into account and that this factor cannot be easily predicted". The Office Action also argues that insufficient guidance and direction is provided to allow one skilled in the art to practice the

claimed invention without undue experimentation. Finally, the Office Action argues that the specification fails to enable the claimed invention because there are no working examples and that one skilled in the art "would be burdened with undue 'painstaking experimentation study'" to practice the claimed invention. Applicant respectfully traverses.

Applicant respectfully submits that there is no requirement for a working example in the patent laws. Further, the case law clearly establishes that what is required is that the specification teaches one skilled in the art how to make and use the claimed invention. As the Patent Office is also aware, the Examiner has the initial burden to establish a reasonable basis to question the enablement of the claimed invention in order to establish a *prima facie* case of lack of enablement. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). *See also In re Morehouse*, 545 F.2d 162, 192 U.S.P.Q. 29 (C.C.P.A. 1976). Further, enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention, *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983), and is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984); *W.L. Gore and Associates v. Garlock, Inc.*, 721 F.2d 1540, 1556, 220 U.S.P.Q. 303, 315 (Fed. Cir. 1983). Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. Further, the quantity of experimentation can be "considerable", "tedious", "laborious", and "time-consuming" as long as the experiments are merely "routine". See *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (B.P.A.I. 1982) ("[t]he test [of enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine."); See also *Ex parte Erlich* 3 U.S.P.Q.2d 1011 (B.P.A.I. 1982).

Applicant respectfully submits that the as-filed specification enables one skilled in the art to practice the claimed invention. For example, the specification clearly sets forth the treatment parameters to be used in protecting an individual against chemotherapy-induced hair loss (alopecia), including the time spans (about 15 to about 120 minutes) and temperatures (about 39°C to about

45°C) to be administered to the individual (see paragraph spanning pages 5-6; page 14, line 12 through to page 16, line 25 and page 19, line 29 through to page 21, line 6). The Patent Office has failed to establish, by an evidentiary showing, that one skilled in the art would not have been able to practice the claimed invention without undue experimentation. Rather, the Office Action makes sweeping statements such as "In the view of the examiner, this is interpreted to say that such treatment parameters cannot be predicted or roughly estimated without conducting such testing". However, in the interest of advancing prosecution in this matter, Applicant submits the attached Declaration of Richard W. Voellmy, Ph.D., Esq. demonstrating that chemotherapy induced hair loss can be reduced or prevented following the teachings of the specification.

As indicated in the accompanying Declaration, animals were randomized into groups and localized heat treatment was provided to one group 7 hours prior to chemotherapy. Localized heat treatment comprised contacting the scalp of the animals with a device that transferred heat (at temperatures of about 39°C to about 45°C) to a specific point on the animal's head for a period of time that ranged from about 15 minutes to about 120 minutes). VP16 (or etoposide; a chemotherapeutic agent) was injected intraperitoneally 2.5 μg/g. A second dose of chemotherapeutic agent was provided 24 hours later and alopecia was recorded 7 days after initiation of chemotherapy. As demonstrated in Exhibit B, page 2, attached to the Declaration, localized heat treatment 7 hours prior to treatment with VP16 prevented alopecia at the site contacted with heat. Additional experiments were conducted with other chemotherapeutic agents with similar results (see Exhibit B, page 3, attached to the Declaration). As illustrated therein, chemotherapy induced alopecia was reduced or prevented in animals treated with taxol (paclitaxel), cyclophosphamide, etoposide, and a combination of cyclophosphamide/adriamycin. Further, administration of heat to the animals resulted in the induction of a heat shock protein response that was associated with protection against chemotherapy-induced alopecia. Non-heat-treated animals showed little induction of heat shock protein (see paragraph 5 of the accompanying Declaration). Thus, Applicant respectfully submits that the teachings of the as-filed specification would have enabled one skilled in the relevant art to practice the claimed invention without undue experimentation and reconsideration and withdrawal of the rejection is respectfully requested.

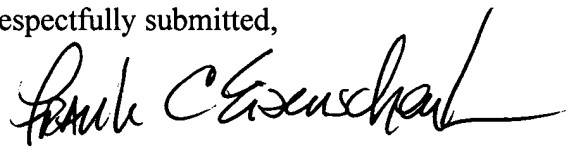
Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks, Applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachment: Declaration of Richard W. Voellmy, Ph.D., Esq. Under 37 C.F.R. §1.132